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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/619,285	07/19/2000	Jeno Gyuris	MIV-109.01	2224

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ROPES & GRAY
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER
DAVIS, NATALIE A

ART UNIT	PAPER NUMBER
1642	10

DATE MAILED: 04/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/619,285	GYURIS ET AL.	
	Examiner	Art Unit	
	Natalie A. Davis	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-79* is/are pending in the application.

4a) Of the above claim(s) *1-27 and 35-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-34 and 49-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's traversal of the election of Group II, claims 28-34 is acknowledged. The traversal is on the ground(s) that the inventions of Groups I, V, and VI may be examined without a serious burden because they are closely related, since Group II is directed to a nucleic acid, which encodes polypeptides of those Groups. This is not found persuasive for reasons indicated in the previous office action, as the Groups have different class/subclass, thus rendering them independent and distinct and a serious burden to search.

The requirement is still deemed proper and is therefore made FINAL.
Claims 28-34 are being examined as belonging to the elected Group II, while claims 1-27 and 35-48 are withdrawn from examination as being drawn to a non-elected invention.

Applicant's amendment filed 8 January 2002 (Paper No: 7) is acknowledged. Accordingly, claims 28-29, 33-34, and 48 are amended and claims 49-79 are new. Claims 28-34 and 49-79 are under examination. Claims 1-27 and 35-48 are withdrawn from examination as being drawn to a non-elected invention.

Applicant indicates that the previous office action did not include claims 47-48 in any of the Groups. Claim 47 should be included in Group III and renumbered claim 48 should be included in Group IV.

Information Disclosure Statement

The information disclosure statement has been considered. A signed copy is attached hereto.***Specification***

1. The disclosure is objected to because of the following informality: The specification makes reference to amino acid sequences on pages 4, and 35-36. All nucleotide sequences with ten or more bases and all unbranched, non-D amino acid sequences with four or more amino acids, provided that there are at least 4 "specifically defined" nucleotides or amino acids embedded within the text of the disclosure must be referenced by sequence identifiers (SEQ ID

NO:). The rules apply to all sequences in a given application, whether claimed or not. Correction is required. See MPEP § 2422.03.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 28-34 and 49-79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 28, 49-50, and 75 are indefinite in the recitation of the phrase "from residues 360-369...". The claim is indefinite because there is no frame of reference in the claim or the specification supplied that will uniquely identify the amino acids of claimed position. maintain

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-34 and 49-79 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

5. The specification does not indicate what biological activity the heterologous peptide that is encoded by the nucleic acid must possess. Accordingly, one of ordinary skill in the art would not know how to make and use the invention because one would not know how to assay and select for the polypeptide since the biological activity of the heterologous peptide has not been defined.

6. The nature of the invention is to a nucleic acid encoding a chimeric polypeptide comprising serum albumin with biologically active heterologous peptide inserted into at least one region replacing one or more residues of the regions into which it is inserted, wherein the chimeric polypeptide exhibits increased biological activity as compared to the heterologous peptide alone, wherein the sequence shares less than 40% identity with a sequence to which it is compared (p. 8). Claims 49-50 are drawn to a nucleic acids encoding chimeric polypeptides which, comprise fragments of serum albumin or anigiogensis-inhibiting polypeptides. There are many heterologous polypeptide molecules, which have less than 40% identity with a sequence to which it is compared and many fragments of serum albumin or anigiogensis-inhibiting polypeptides that may or may not perform the same biological functions and the specification does not give any guidance to which molecules will exhibit the biological activities as the claimed, or any guidance as to which regions of amino acid sequence are responsible for biological activity and thus, must be preserved so the molecule will function as claimed. Thus, it would be an undue burden to one of ordinary skill in the art to assay for claimed sequences, which are capable of functioning as contemplated. One cannot extrapolate the teachings of the specification to the breadth of the claims because the claims are broadly drawn to any nucleic acids encoding a chimeric polypeptide comprising a heterologous polypeptide and fragments of serum albumin or anigiogensis-inhibiting polypeptides and applicant has not enabled all of these types of modifications because it has not been shown that these polypeptides are capable of functioning as that which is being disclosed. Reasonable correlation must exist between the breadth of the claims and the enablement set forth, and it cannot be predicted from the disclosure as to which polypeptides and fragments should be isolated.

7. Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, conservative replacement of a single "lysine" reside at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding

and biological activity of the protein (Burgess et al., J of Cell Bio. 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cellular Biology 8:1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed sequence can be tolerated that will allow the protein to function as claimed. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions. Residues that are directly involved in protein functions such as binding will certainly be among the most conserved (Bowie et al. Science, 247:1306-1310, 1990, p. 1306, col.2). Therefore, in view of the unpredictability in the art, lack of working examples, the breadth of the claims, and insufficient guidance as indicated above, one of skill in the art would not be able to practice the claimed invention because undue experimentation would be required.

8. Claim 58 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

drop

Vas-Cath Inc. v. Mahurkar (CA FC) 19 USPQ2d 1111 (6/7/1991) clearly states that "written description" of invention required by first paragraph of 35 U.S.C. 112 is separate and distinct from that paragraph's requirement of enabling disclosure, since description must do more than merely provide explanation of how to "make and use" invention; applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry,

whatever is presently claimed. An applicant shows possession by describing the claimed invention with all it limitations using such descriptive means as words, structures, diagrams, and formulas. Also, description of an actual reduction to practice, or by showing the invention was "ready for patenting," or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention at the time of filing.

9. The elected claim is drawn to a nucleic acid that encodes a chimeric polypeptide wherein the heterologous peptide sequenc binds to an orphan receptor. The specification does not disclose any objective evidence regarding the isolation of and assaying of the claimed nucleic acid, the successful binding of a heterologous polypeptide to an orphan receptor. In addition, no other examples are disclosed that conveys to one of skill in the art that the applicant was in possession of the claimed nucleic acid. There is no actual reduction to practice, sufficient descriptive information, such as definitive structural features, which are critical to activity, or complete detailed description of the function of claimed invention indicating that the claimed nucleic acid were indeed isolated, produced, and assayed for the uses disclosed. Thus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Natalie A. Davis whose telephone number is 703-308-6410. The examiner can normally be reached on M-F 8-5:30 (every other Friday off).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa PhD can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4315 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Natalie A. Davis, PhD
April 7, 2002